I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with § 1.6(a)(4).

Dated: May 20, 2008 2008 Signature: /David A. Gass #38,153/
(David A. Gass)

Docket No.: 19036/40796
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Yuka Matsui

Application No.: 10/561,629 Confirmation No.: 8420

Filed: (national stage application of PCT/JP2004/008710, filed June 21, 2004) Art Unit: Not Yet Assigned

For: OPHTHALMIC COMPOSITION Examiner: Not Yet Assigned

SECOND RENEWED PETITION UNDER 37 CFR 1.47(B)

MS PCT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In response to the Decision on assignee's petitions under 37 CFR 1.47(b) (renewed petition) and 1.59(b), mailed March 24, 2008, the assignee submits the following second renewed petition under 37 CFR 1.47(b). The Decision dismissed the assignee's renewed petition under 37 CFR 1.47(b) and set a two month extendable period within which to request reconsideration. This second renewed petition is timely. Reconsideration is requested.

Except as explained herein and modified by the petition under 1.59(b), the assignee continues to rely on material filed in support of the original and renewed petition and incorporates such material herein by reference.

The Decisions to dismiss assignee's initial and renewed petition cited six requirements for a petition under 37 CFR 1.47(b): (1) the petition fee; (2) factual proof of the inventor's refusal to sign the declaration or of diligent effort to reach an unavailable inventor; (3) a statement of last known address of the inventor; (4) an oath or declaration by the 37 CFR 1.47(b) applicant on behalf of or as agent for the non-signing inventor; (5) proof that the

37 CFR 1.47(b) applicant has sufficient proprietary interest in the application; and (6) a showing that such action is necessary to preserve the rights of the parties or to prevent irreparable damage. The Decision on (renewed) Petition Under 37 CFR 1.47(b) stated that items (1)-(4) and (6) have been met (and no additional petition fee is due with this request) but alleged that item (5) has not. This paper presents further support for item (5) and it is respectfully requested that this renewed petition under 37 CFR 1.47(b) be granted.

A. The assignment of the priority application and the substantive identity between the priority and PCT applications together demonstrate that the petitioner is assignee of the invention, satisfying the requirements of Rule 1.47(b)

In support of a showing of sufficient proprietary interest for item (5), the assignee previously submitted a translation of Japanese Application No. 2003-176965, filed June 20, 2003, as requested by the Petitions Office in its prior Decision, mailed June 11, 2007. As demonstrated in the original petition, Inventor Matsui assigned all of her intellectual property rights throughout the world, including her rights to obtain patents, to Kobayashi Pharmaceutical with respect to Japanese Application No. 2003-176965 and *the invention* titled "Ophthalmic Composition" described therein. The assignment was recorded with the U.S. Patent Office at Reel/Frame No. 018868/0382. The current U.S. application is a national stage application of PCT application No. PCT/JP2004/008710, filed June 21, 2004, which claims priority to assigned Japanese Application No. 2003-176965.

Applicants first renewed petition, submitted October 9, 2007, provided a claim chart showing that the claims in the current U.S. (and PCT) application are directed to an invention that was fully described in the Japanese priority application. Because the invention of the priority application was assigned to petitioner, and the PCT application is claiming the invention of the priority application, the petitioner has demonstrated that petitioner is "a person to whom an inventor has assigned the invention" as required by Rule 1.47(b). Item (5) thus was satisfied in the renewed petition.

The Patent Office, in its dismissal of March 24, states that this showing of support of the claims as currently pending, does not address "that there is no matter in the

international application which is not in the priority application. Such matter could be added to the claims by amendment at a later date." (Dismissal, p 2.)

B. A comparison between the specifications of the provisional and PCT applications demonstrate that there is no unassigned invention that would be claimed by amendment during prosecution, because the two specifications are essentially identical in substance.

In response to the new concerns raised in the Decision, the petitioner/assignee submits herewith a "redline" comparison of the specification portion of the English translation of the Japanese priority application and the English translation of the PCT application (Appendix 1). (As noted above, the assignee has previously shown the clear support for the current claims in the Japanese priority application in its first Renewed Petition, so this comparison pertains to the specification only.) In the comparison, the color blue identifies added text that is found in the PCT but that was not in the Japanese priority application. The color green identifies text that was in the Japanese priority application but was *moved to a different position* in the application. (If the Patent Office needs a paper version to assist it in visualizing the color document, please contact the undersigned.) This appended redline comparison shows that there are no substantial differences between the substantive contents of the priority and the PCT applications. Therefore, the subject matter of the assigned Japanese priority application and the PCT application are substantively essentially identical. By virtue of the assignment of relating to the priority application and its invention, petitioner Kobayashi also is properly the assignee of the invention in the present application, and has sufficient proprietary interest in the present application to grant a petition under Rule 1.47(b).

Therefore, because Ms. Matsui executed an assignment of the priority document assigning her rights in the invention of the priority document to Kobayashi; the claims of the present application are fully supported in the priority document; and there is no substantial difference between the priority document and the PCT application, petitioner Kobayashi has the requisite proprietary interest in the current application to file this application. Thus, the petition should now be granted.

C. The allegation that there may be no unassigned subject matter is contrary to the plain language of Rule 1.47 and is an improper basis for dismissing the present petition.

Moreover, assignee submits that the Patent Office has applied an incorrect standard for "element (5)" of the petition (pertaining to "sufficient proprietary interest"). The rule states that a petition under 37 CFR 1.47(b) can be undertaken by "a person to whom an inventor has assigned or agreed in writing to assign the invention, or who otherwise shows sufficient proprietary interest in the matter." (Emphasis added.) In the prior renewed petition under 37 CFR 1.47(b), the assignee showed support for the claims of the present application in the Japanese priority document, which the inventor explicitly assigned to the assignee (see Reel/Frame No. 018868/0382).

Rule 1.47(b) by its plain language is satisfied by a showing of assignment of "the invention." It is axiomatic that the claims define "the invention." (See 35 USC 112, second paragraph "[t]he specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention."). Thus, the requirements of Rule 1.47(b) were satisfied by the first renewed petition, by which the petitioner has shown it is the assignee for the invention defined by the pending claims. Rule 1.47(b) is silent with respect to the significance of any potential claim amendments that may be made during prosecution.

Even if there were subject matter in the PCT application not found in the assigned Japanese priority application, the assignee has certainly shown a "sufficient proprietary interest" to satisfy Rule 1.47(b). The Decision suggests that a showing of a *complete* proprietary interest is necessary, but nothing in the rule requires a showing of *complete* proprietary interest. By analogy, Rule 1.47(a) permits a joint applicant (with less than 100% interest) to make an application on behalf of himself and a non-signing inventor. Thus, an inventor that is not an owner of the entirety of an invention or entirety of an application can file a petition under Rule 1.47(a), proving that Rule 1.47 clearly does not stand for the proposition that a 100% proprietary interest is required to prosecute an application, if an inventor refuses to cooperate.

The plain language of Rule 1.47(b) requires the same conclusion. The rule specifies that "whenever all of the inventors refuse to execute an application...a person to whom an inventor has assigned...the invention...may make application." (Emphasis added.) The use of "all" and "an" makes clear that an assignee of less than the entire interest in a patent application (e.g., by virtue of receiving only one of multiple inventors' rights) is permitted by Rule 1.47(b) to make application for the patent. There is no basis in the rule or the cases cited by the Decision for the standard applied to deny the renewed petition: "it is not clear that there is no matter in the international application which is not in the priority application."[1] In fact, the last sentence of Rule 1.47(a) provides a safeguard that permits an inventor to subsequently join in the application, which would protect an inventor who had a theoretical interest in an application that was completely or partly assigned.

Not only is the "no matter" standard used to dismiss the petition unrelated to, and stricter than, the plain language of the rule, it also could not be satisfied by any assignee of any application, even after showing an assignment by the inventors of an application that is the subject of a Rule 1.47(b) petition. Even then, there would be a possibility that claim amendments during prosecution could be introduced directed to subject matter in the application that is not the invention of assigning inventors. (Every patent application, in the course of describing an invention and how to use it, also describes elements, reagents, or other details that are not themselves "the invention.") The PTO has other rules (besides Rule 1.47) for addressing such concerns. (Compare Rules 1.48(b) and 1.48(c).) Rule 1.47 is not a rule designed to police future claim amendments, and contains no requirement that a petitioner show entitlement to claim all subject matter that could be introduced into a claim by way of amendment.

[1] It should be noted that the MPEP §409.03 quoted in the Decision only requires a showing of "sufficient proprietary interest" in circumstances where the invention has not been assigned and there is no written agreement to assign. That is plainly not the situation here.

It is submitted that the assignee has shown sufficient evidence of inventor Matsui's refusal to sign an inventor's declaration and has supplied all other required documents and evidence for a petition under 37 CFR 1.47(b). It is respectfully requested that the petition under 37 CFR 1.47(b) be granted. If the Patent Office or Petitions Officer wishes to discuss this request further, he is invited to contact the undersigned at the telephone number listed below.

Dated: May 20, 2008

Respectfully submitted,

Signature: David A. Gass #38,153/

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OPHTHALMIC COMPOSITION

[TECHNICAL FIELD ~~WHERE THE INVENTION BELONGS~~]

The present invention relates to an ophthalmic composition. More particularly, of an ophthalmic composition containing pyridoxine hydrochloride, the present invention relates to the ophthalmic composition which exhibits the reduced irritation to eyes. Furthermore, the present invention relates to a process for alleviating irritation to eyes with an ophthalmic composition including pyridoxine hydrochloride.

~~0002~~

~~PRIOR~~[BACKGROUND ART]

In the development of pharmaceutical products for use in the ophthalmologic field, irritations to the ophthalmic mucosa and discomfort have to be always considered in addition to the medical effect thereof. Hence, with regard to various types of active components used in the conventional ophthalmic compositions, some processes for removing or alleviating and moderating the irritation have been proposed.

~~0003~~ For example, ~~Patent Literature~~Prior Art 1 discloses a process for moderating with cyclosporine irritations to mucosa of eyes, nose or the like due to cetirizine to be acted as an antiallergic agent; ~~Patent Literature~~Prior Art 2 discloses a process for moderating irritations to eyes with 2-(2-fluoro-4-biphenylyl)propionic acid which is used as an anti-inflammatory agent by blending one or two or more of polyvinyl alcohol, methyl cellulose, carboxymethyl cellulose, hydroxyethyl cellulose, hydroxypropyl methyl cellulose and sodium chondroitin sulfate in an amount of 0.01 to 2% to form a composition with the pH 5-8 so adjusted; ~~Patent Literatures~~Prior Arts 3 and 4 disclose a process for moderating irritations to eyes with 2-acetyl-1-(2-hydroxy-8-isopropylaminopropoxy)benzofuran which is used as an intraocular pressure decreasing agent or a therapeutic agent for glaucoma by blending (A) 0.001 to 0.1% benzalkonium chloride or benzethonium chloride, and (B) at least one compound of polyvinyl alcohol, methyl cellulose, carboxymethyl cellulose and hydroxyethyl cellulose in an amount of 0.02 to 2 w/v%, or hydroxypropyl methyl cellulose in an amount of 0.01 to 1 w/v% to form a composition with the pH 5-8 so adjusted; and, ~~Patent Literature~~Prior Art 5 disocloses a process for moderating irritations to eyes with lower alcohol such as ethanol which is used as a refrigerant by blending a saccharide such as mannitol, xylitol, glucose and maltose.

~~0004~~

Accordingly, ~~various~~variable types of irritating components are available, and under current circumstances, processes for removing or alleviating and moderating the wide variety of different irritations have been studied and proposed depending on the type thereof.

~~0005~~

~~Patent Literature 1~~Prior Art 1: Japanese Patent Provisional Publication No. 6-239748.

~~0006~~

~~Patent Literature 2~~Prior Art 2: Japanese Patent Provisional Publication No. 57-102817.

~~0007~~

~~Patent Literature 3~~Prior Art 3: Japanese Patent Provisional Publication No. 56-39013.

~~0008~~

~~Patent Literature 4~~Prior Art 4: Japanese Patent Provisional Publication No. 57-16817.

~~0009~~

~~Patent Literature 5~~Prior Art 5: Japanese Patent Provisional Publication No. 2001-261578.

~~0010~~

[DISCLOSURE OF THE INVENTION]

~~[~~PROBLEMS TO BE SOLVED BY THE INVENTION~~]~~

An object of the present invention is to provide a process for alleviating an irritation or discomfort to eyes with pyridoxine hydrochloride which has often been used in ophthalmic-pharmaceutical compositions to expect the moderating effects of asthenopia, and an ophthalmic composition which alleviates an irritation to eyes according to the process.

~~0011~~

~~ELEMENTS~~[MEANS TO SOLVE THE PROBLEMS~~]~~

The present inventor investigated to develop an ophthalmic composition to moderate asthenopia, and discovered that an ophthalmic composition containing pyridoxine hydrochloride as an active component to moderate asthenopia may cause an unpleasant irritation to the ophthalmic mucosa. Hence, as a consequence of elaborate investigations for eliminating such problems and for obtaining a desired ophthalmic composition as described above, it was found that preparation of an ophthalmic composition containing the combined components of chondroitin sulfate salt and cellulose based polymer compound, in addition to pyridoxine hydrochloride, enables an ophthalmic composition to moderate asthenopia without unpleasant irritation through alleviating or removing irritation to be generated from pyridoxine hydrochloride. Furthermore, the effect of alleviating or removing the unpleasant irritation allows using a large amount of pyridoxine hydrochloride, thereby, an ophthalmic composition may then moderate asthenopia remarkably. The present invention was accomplished based on such

investigation results.

~~0012~~ Accordingly, merits of the present invention are as follows.

~~Item 1.~~ (1) An ophthalmic composition which comprises pyridoxine hydrochloride, chondroitin sulfate salt and cellulose based polymer compound.

~~Item 2.~~ (2) The ophthalmic composition according to the item (1) wherein said cellulose based polymer compound is at least one compound selected from hydroxyethyl cellulose, methyl cellulose, and hydroxypropyl methyl cellulose.

~~Item 3.~~ (3) A process for alleviating an irritation to eyes with an ophthalmic composition containing pyridoxine hydrochloride, the process comprises blending chondroitin sulfate salt and cellulose based polymer compound together with an ophthalmic composition containing pyridoxine hydrochloride.

~~Item 4.~~ (4) The process for alleviating an irritation according to the item (3) wherein said cellulose based polymer compound is at least one compound selected from hydroxyethyl cellulose, methyl cellulose, and hydroxypropyl methyl cellulose.

~~0013~~

~~EMBODIMENTS~~

[EFFECTS OF THE INVENTION]

The ophthalmic composition of the present invention has an effect to moderate asthenopia by pyridoxine hydrochloride used as an active component thereof, and an irritation to eyes with pyridoxine hydrochloride is also alleviated or removed by the combined components of chondroitin sulfate salt and cellulose based polymer compound. Therefore, according to the present invention, an ophthalmic composition can be used without unacceptable sense, and an effect to moderate asthenopia can be offered. Moreover, according to the present invention, a process for removing or alleviating an irritation to eyes with pyridoxine hydrochloride can be provided.

[BEST MODE FOR CARRYING OUT THE INVENTION]

(1) Ophthalmic Composition

The ophthalmic composition of the present invention uses pyridoxine hydrochloride as an active component, and the combined components of chondroitin sulfate salt and cellulose based polymer allow to accompolish the merits of the present invention to provide an ophthalmic composition composition which can be used without unacceptable sense and can offer an improved effect to moderate asthenopia due to pyridoxine hydrochloride, through alleviation or removal of the irritation resulting from the aforementioned pyridoxine hydrochloride.

~~0014~~

Chondroitin sulfate salt to be used in the present invention is not particularly limited as long as it is a pharmaceutically acceptable salt of chondroitin sulfate,

but may be usually sodium chondroitin sulfate. An amount of the chondroitin sulfate salt to be blended into the ophthalmic composition is not particularly limited as long as the merit of the present invention is accomplished, but illustrative range thereof may be 0.001 w/v% or more, preferably 0.001 to 0.5 w/v%, and more preferably 0.005 to 0.5 w/v% in 100 w/v% of the ophthalmic composition. Also, exemplary ratio to pyridoxine hydrochloride to be blended into the ophthalmic composition may be 0.01 to 2,000 parts by weight, preferably 0.05 to 2,000 parts by weight, and more preferably 0.05 to 500 parts by weight per 1 part by weight of pyridoxine hydrochloride.

[0015]

Furthermore, specific examples of the cellulose based polymer compound which may be used in the present invention include alkyl cellulose such as methyl cellulose, ethyl cellulose and carboxymethyl cellulose; hydroxyalkyl cellulose such as hydroxyethyl cellulose, hydroxyethyl methyl cellulose, hydroxypropyl cellulose and hydroxypropyl methyl cellulose. Preferably, it may be methyl cellulose, hydroxypropyl methyl cellulose, or hydroxyethyl cellulose, and more preferably, methyl cellulose or hydroxypropyl methyl cellulose. These may be used alone, or in optional combination of two or more of them.

[0016]

An amount of the blended cellulose based polymer compound to be used in the ophthalmic composition is not particularly limited as long as the merit of the present invention is accomplished. In general, the amount thereof can not be determined regularly, because it may vary depending on the type of the cellulose based polymer compound as actually used, but can be selected and adjusted ad libitum to fall within the range of 0.01 to 10 w/v%, preferably 0.01 to 5 w/v%, and more preferably 0.05 to 5 w/v% in 100 w/v% of the ophthalmic composition as a reference. Also, exemplary ratio to pyridoxine hydrochloride blended into the ophthalmic composition may be 0.1 to 10,000 parts by weight, preferably 0.1 to 5,000 parts by weight, and more preferably 0.1 to 200 parts by weight per 1 part by weight of pyridoxine hydrochloride. Moreover, it is desired to adjust the ratio of the cellulose based polymer compound per 1 part by weight of the chondroitin sulfate salt blended into the ophthalmic composition appropriately to be 0.02 to 10,000 parts by weight, preferably 0.02 to 5,000 parts by weight, and more preferably 0.02 to 1,000 parts by weight.

[0017]

The concentration of pyridoxine hydrochloride in the ophthalmic composition of the present invention may vary widely depending on the particular use of the composition (either pharmaceutical use or the other use) and extent of the asthenopia to be ameliorated, but may be usually 0.001 w/v% or more, preferably 0.001 to 1 w/v%, and more preferably 0.001 to 0.1 w/v%.

[0018]

The ophthalmic composition of the present invention is preferably adjusted to the pH range which is generally acceptable for ophthalmic applications. Specifically, pH may fall within the range of from 4 to 9, preferably 5 to 8, and more preferably 5.5 to 8.

[0019]

Furthermore, the ophthalmic composition of the present invention is preferably adjusted to the osmotic pressure range which is generally acceptable for ophthalmic applications. Specifically, it is preferably adjusted to be a pressure ratio falling within the range of 0.5 to 5, and more preferably within the range of the pressure ratio of 0.8 to 2. For adjusting the osmotic pressure, for example, any method usually adopted in preparation of eye drops can be used in a similar manner.

[0020]

Besides pyridoxine hydrochloride, any component to be acted to moderate asthenopia may be blended in the ophthalmic composition of the present invention as long as the merit of the present invention is not impaired. Also, other pharmaceutically effective components commonly used in ophthalmologic field may also be blended ad libitum.

[0021]

Such pharmaceutically effective components are not limited, and illustrative examples thereof include decongestants (e.g., naphazoline hydrochloride, tetrahydrozoline hydrochloride, phenylephrine hydrochloride, epinephrine hydrochloride and the like), antiphlogistic, astringent drugs (e.g., neostigmine methylsulfate, ε-amino caproic acid, allantoin, berberine chloride, zinc sulfate, lysozyme chloride, sodium azulene sulfonate, dipotassium glycyrrhizinate and the like), antiallergic agents (diphenhydramine hydrochloride, isopenzyl hydrochloride, chlorpheniramine maleate, sodium cromoglycate and the like), vitamins other than pyridoxine hydrochloride (e.g., vitamin B_2, vitamin B_{12}, vitamin A, vitamin E, calcium pantothenate and the like), amino acids (potassium L-aspartate, magnesium L-aspartate, aminoethylsulfonic acid and the like), sulfa drugs (e.g., sulfamethoxazole, sulfisoxazole, sulfisomidine and the like), bacteriocides (sulfur, isopropylmethyl phenol, hinokithiol and the like), topical anesthetics (lidocaine, lidocaine hydrochloride, procaine hydrochloride, dibucaine hydrochloride and the like), inorganic salts (e.g., potassium chloride, sodium chloride, sodium bicarbonate and the like), thickening agents (polyvinyl alcohol, polyvinyl pyrrolidone, carboxymethyl cellulose, hyaluronic acid, glucose and the like), but not limited thereto.

[0022]

A variety of additives (e.g., solubilization auxiliary agents, isotonizing agents, stabilizing agents, chelating agents, pH adjusting agents, refrigerants, preservatives, and thickening agents) as well as a carrier (e.g., buffer agents, and ointment bases) which may be generally used in ophthalmic compositions can also be blended, in addition to

the aforementioned essential components, into the ophthalmic composition of the present invention in the range not to compromise the merit of the present invention.

[0023]

Illustrative examples of the solubilization auxiliary agent include polyethylene glycol, propylene glycol and the like; ~~tonicity~~isotonizing agent include sodium chloride, potassium chloride, sorbitol, mannitol, glycerin and the like; stabilizing agent include sodium edetate, cyclodextrin, sulfite, citric acid or salts thereof, and the like; the chelating agent include sodium edetate, sodium citrate and the like; pH adjusting agent include hydrochloric acid, citric acid or salts thereof, boric acid or salts thereof, phosphoric acid or salts thereof, acetic acid or salts thereof, tartaric acid or salts thereof, sodium hydroxide or potassium hydroxide, and the like; refrigerant include monoterpenoid compounds such as menthol, camphor, borneol, geraniol, cineol, limonene and eugenol, or peppermint oil, bergamot oil, eucalyptus oil, fennel oil, cool mint, and the like; examples of the preservative include paraoxybenzoic acid esters, benzalkonium chloride, chlorobutanol and the like; and moreover, thickening agent include polyvinyl alcohol, polyvinylpyrrolidone, carboxymethyl cellulose, hyaluronic acid, glucose and the like.

[0024]

Furthermore, illustrative examples of the buffer agent include phosphoric acid or salts thereof (e.g., sodium monohydrogen phosphate and the like), boric acid or salts thereof (e.g., borax and the like), citric acid or salts thereof (e.g., sodium citrate and the like), tartaric acid or salts thereof (e.g., sodium tartrate and the like), gluconic acid or salts thereof (e.g., sodium gluconate and the like), acetic acid or salts thereof (e.g., sodium acetate and the like), various amino acids, and the like.

[0025]

Moreover, illustrative examples of the base for use in the ophthalmic ointment include, for example, white petrolatum, liquid paraffin, carboxymethyl cellulose, macrogol, carboxyvinyl polymer, and the like.

[0026]

These compositions can be of any formulation generally used in ophthalmic compositions. Examples of such formulation include, for example, aqueous solutions, suspensions, emulsions, gelatinous materials, ointments and the like. Also, the dosage form is not particularly limited, but any form such as eye drops (including those for contact lenses), ophthalmic ointments, or eye lotions may be permitted. Furthermore, a solid type formulation prepared before use may be permitted which is obtained by solidifying the composition of the present invention by a process such as freeze-drying followed by forming a solid formulation like powder, granule or tablet form to be used after dissolution or the like in purified water upon use.

[0027]

The process for preparing the ophthalmic composition of the present invention is not particularly limited, but may be prepared according to common procedures for ophthalmic compositions. For example, the composition can be prepared by dissolving each component described above in water such as sterile purified water or ion exchanged water, or in a mixed solvent of the water and a lower alcohol such as ethanol, and thereafter, pH or osmotic pressure of the composition is adjusted appropriately with a pH adjusting agent, an isotonizing agent or the like.

[0028]

Preferrably, the ophthalmic composition of the present invention is administered, for example, into an adult in the form of an eye drops by dropping to eye one to few drop(s) per once approximately 3 to 6 times per day.

[0029]

~~[EFFECTS OF THE INVENTION]~~

~~The ophthalmic composition of the present invention has an effect to moderate asthenopia by pyridoxine hydrochloride used as an active component thereof, and an irritation to eyes with pyridoxine hydrochloride is also alleviated or removed by the combined components of chondroitin sulfate salt and cellulose based polymer compound. Therefore, according to the present invention, an ophthalmic composition can be used without unacceptable sense, and an effect to moderate asthenopia can be offered. Moreover, according to the present invention, a process for removing or alleviating an irritation to eyes with pyridoxine hydrochloride can be provided.~~

[0030]

~~[~~[EXAMPLES]~~]~~

Hereinafter, the present invention will be illustrated in detail by way of Example and Relative, but the present invention is not limited anyhow by the disclosure thereof.

[0031]

Examples 1-2, Relatives 1-6 and Control

Eye drops made from the prescription shown in Table 1 were prepared (Examples 1-2, Relatives 1-6, Control), and evaluated on the irritation when they were dropped in eyes. The viscosity of the eye drops is indicated as a value determined with B type viscometer at 20°C.

[0032]

Irritation to eyes was evaluated with sensory test wherein ten persons of adult men and women were participated. Each person rated irritation according to the following standard for eye drops of each prescription and evaluated it on the basis of the total points.

[0033]

<Evaluation on Moderation of Irritation>

No irritation experienced at all;	10 points
Irritation not experienced well;	5 points
Undecidable;	0 point
Irritation somewhat experienced;	-5 points
Irritation experienced;	-10 points

[0034]

The results are also shown in Table 1.

[0035] [Table 1]

Amount blended (mg/100 ml)

	Example 1	Example 2	Relative 1	Relative 2	Relative 3	Relative 4	Relative 5	Relative 6	Control
Pyridoxine Hydrochloride	50	50	50	50	50	50	50	50	50
HPMC	300	-	300	-	300	500	-	300	-
Methyl Cellulose	-	300	-	-	500	-	-	100	-
Sodium Chondroitin Sulfate	500	500	-	500	-	-	800	-	-
Chlorpheniramine Maleate	15	15	15	15	15	15	15	15	15
Boric Acid	600	600	600	600	600	600	600	600	600
Glycerin	1750	1750	1750	1750	1750	1750	1750	1750	1750
Benzalkonium Hydrochloride	2	2	2	2	2	2	2	2	2
Disodium Edetate	5	5	5	5	5	5	5	5	5
Polysorbate 80	10	10	10	10	10	10	10	10	10
Sodium Hydroxide (pH adjusting agent)	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.
pH	5.7	5.7	5.7	5.7	5.7	5.7	5.7	5.7	5.7
Viscosity (cP)	11.1	10.2	8.67	1.81	124	25.6	2.28	14.0	1.16
Irritation to Eyes	100	80	-60	-60	-45	-55	-55	-40	-70

[0036] In the Table, "HPMC" means hydroxypropyl methyl cellulose. As shown in Table 1, irritation to eyes with pyridoxine hydrochloride (Control) was revealed to be markedly alleviated or removed by using the combined components of the cellulose based polymer compound and sodium chondroitin sulfate (Examples 1 and 2). Furthermore, this effect was not exerted unless both the cellulose based polymer compound and sodium chondroitin sulfate were used, while the cellulose based polymer compound alone (Relatives 1 and 4) or combination thereof (Relatives 3 and 6), and sodium chondroitin sulfate alone (Relatives 2 and 5) exhibited no effect at all. Moreover, from the results of Relatives 1 and 4, Relatives 2 and 5, and Relatives 3 and 6 shown in Table 1, it was elucidated that the viscosity of the ophthalmic composition does not affect the moderation of irritation to eyes with pyridoxine hydrochloride.

[0037]

Example 3

An ophthalmic composition in the form of ointment was prepared according to the following prescription.

[0038]

Pyridoxine Hydrochloride	100 mg
HPMC	500
Sodium Chondroitin Sulfate	500
Sodium Cromoglycate	1,000
Carboxymethyl Cellulose	4,000
Glycerin	2,660
Benzalkonium Chloride	5
Polysorbate 80	20
Sodium hydroxide	q.s. (pH 5.7)
Sterile Purified Water	Residual amount
Total	100 mL

[0039]

Example 4

An ophthalmic solution was prepared according to the following prescription.

[0040]

Pyridoxine Hydrochloride	5 mg
HPMC	1,000
Sodium Chondroitin Sulfate	50
Disodium Glycyrrhizinate	5
Boric Acid	1,000
Benzalkonium Chloride	5
Disodium Edetate	5
Polysorbate 80	20
Sodium Hydroxide	q.s. (pH 5.7)
Sterile Purified Water	Residual amount
Total	100 mL

[0041]

Example 5

An eye drop was prepared according to the following prescription.

[0042]

Pyridoxine Hydrochloride	50 mg
HPMC	300
Sodium Chondroitin Sulfate	500
Chlorpheniramine Maleate	15
Boric Acid	600
Glycerin	1,750
Benzalkonium Chloride	2
Disodium Edetate	5
Polysorbate 80	10
Sodium Hydroxide	q.s. (pH 5.7)
Sterile Purified Water	Residual amount
Total	100 mL